Patent

#### Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application: Listing of Claims:

1-12. (canceled)

- 13. (currently amended) A method of distinguishing P-gp/MRP P-gp or MRP mediated multiple drug resistance from BCRP mediated or other non P-gp/non-MRP multiple drug resistance in cancer cells exhibiting such resistance which comprises:
- a. contacting P-gp/MRP multidrug resistant cancer cells P-gp mediated multiple drug resistant cancer cells S1-B1-20 or MRP mediated multiple drug resistant cancer cells HL-60/AR with a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death:
- b. contacting said P-gp/MRP P-gp or MRP mediated multidrug resistant cancer cells with a test chemosensitizing reversal agent selected from compounds of Formula (I)

$$R^{1} \xrightarrow{N} R^{2} \xrightarrow{R^{3}} O \xrightarrow{N} O R^{6}$$
(I)

wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

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m is an integer of 1 to 6;

v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

or a pharmaceutically acceptable salt thereof, Fumitremorgin A, Fumitremorgin B and Fumitremorgin C and a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

- c. contacting BCRP <u>mediated</u> <u>multidrug</u> <u>multiple</u> drug resistant <u>S1-M1-3.2</u> cancer cells with a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;
- d. contacting said BCRP <u>mediated multiple drug multidrug</u> resistant <u>S1-M1-3.2</u> cancer cells with said <del>test</del>-chemosensitizing reversal agent and a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

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e. contacting non-P-gp/non-MRP-multidrug resistant cancer cells with a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

f. contacting said non P-gp/non MRP multidrug resistant cancer cells with said test chemosensitizing reversal agent and a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

- g. e. distinguishing P-gp/MRP, P-gp or MRP from BCRP or other non-P-gp/non MRP mediated multiple drug resistance by comparing cancer cell death of step a to step b, and step c to step d and step e to step f wherein an increase in cell death in comparing step c to d and step e to f shows said test chemosensitizing reversal agent is a chemosensitizing reversal agent having activity in BCRP mediated or other non-P-gp/non-MRP multiple drug resistance.
- 14.(Previously presented) The method according to claim 13 wherein the increase in cancer cell death by addition of the test chemosensitizing reversal agent is about 22% or above.
- 15. (currently amended) The method according to claim 13 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, doxorubicin, <u>paclitaxel</u> and topotecan.
- 16. (canceled)
- 17. (original) The method according to claim 13 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.
- 18. (currently amended) A method of distinguishing P-gp/MRP P-gp or MRP mediated multiple drug resistant cancer cells multiple drug resistance from BCRP mediated or other non-P-gp/non-MRP-multiple drug resistance in cancer cells exhibiting such resistance which comprises:
- a. contacting P-gp/MRP P-gp mediated multiple drug resistant cancer cells S1-B1-20 or MRP mediated multiple drug resistant cancer cells HL-60/AR multidrug resistant cancer cells with a chemotherapeutic agent to which said cancer cells are resistant and measuring chemotherapeutic agent accumulations in the cell;
- b. contacting said P-gp mediated multiple drug resistant cancer cells S1-B1-20 or MRP mediated multiple drug resistant cancer cells HL-60/AR multidrug resistant cancer cells with an effective amount of a test-chemosensitizing reversal agent selected from compounds of Formula (I)

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# wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

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m is an integer of 1 to 6; v is an integer of 1 to 4; R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

or a pharmaceutically acceptable salt thereof, Fumitremorgin A, Fumitremorgin B and Fumitremorgin C and a chemotherapeutic agent to which said cancer cells are resistant and measuring chemotherapeutic agent accumulations in the cell;

- c. contacting BCRP mediated multidrug resistant cancer cells <u>S1-M1-3.2</u> with a chemotherapeutic agent to which said cancer cells are resistant and measuring chemotherapeutic agent accumulations in the cell;
- d. contacting said BCRP mediated multidrug resistant cancer cells <u>S1-M1-3.2</u> with said test chemosensitizing reversal agent and a <u>and said</u> chemotherapeutic agent to which said cancer cells are resistant and measuring chemotherapeutic agent accumulations in the cell;
- e. contacting non P-gp/non MRP multidrug resistant cancer cells with a chemotherapeutic agent to which said cancer cells are resistant and measuring chemotherapeutic agent accumulations in the cell;
- f. contacting said non-P-gp/non MRP multidrug resistant cancer cells with said test chemosensitizing reversal agent and a chemotherapeutic agent to which said cancer cells are resistant and measuring chemotherapeutic agent accumulations in the cell;
- g. distinguishing P-gp/MRP, e. distinguishing P-gp mediated multiple drug resistance or MRP mediated multiple drug resistance from BCRP mediated or other non P-gp/non MRP multiple drug resistance by comparing measured chemotherapeutic agent accumulations in the cell of step a to step b, and step and step c to step d and step e to step f wherein an increase in chemotherapeutic agent accumulations in the cell in comparing step a to b, step c to d and step e to f distinguishes whether said test chemosensitizing reversal agent is a chemosensitizing reversal agent having P-gp/MRP or activity in BCRP mediated or other non P-gp/non MRP multiple drug resistance.
- 19.(currently amended) The method according to claim 18 wherein the ehemotherapeutic agent used is one to which the cancer cells are resistant increase in chemotherapeutic agent accumulation by addition of the test chemosensitizing reversal agent is about 13 % or above.
- 20. (currently amended) The method according to claim 18 wherein the chemotherapeutic agent is selected from the group consisting of mitoxantrone, <u>and doxorubicindoxorubicin</u>, and topotecan.

#### 21. (canceled)

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### 22. (canceled)

23. (original) The method according to claim 18 wherein the chemosensitizing reversal agent is administered prior to, concurrently with, or after administration of the chemotherapeutic agent.

- 24. (currently amended) A method of determining the presence and magnitude of cancer cell BCRP <u>mediated</u> multiple drug resistance or other non P gp/non MRP multiple drug resistance in cancer cells exhibiting such resistance which comprises:
- a. contacting BCRP mediated multidrug resistant <u>S1-M1-3.2</u> cancer cells with a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;
- b. contacting said BCRP multidrug resistant cancer cells with a test chemosensitizing reversal agent selected from compounds of Formula (I)-

#### wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

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$$\begin{array}{c|c} & & \\ & &$$

m is an integer of 1 to 6;

v is an integer of 1 to 4;

## $R^4$ , $R^5$ and $R^6$ are hydrogen;

or a pharmaceutically acceptable salt thereof, Fumitremorgin A, Fumitremorgin B and Fumitremorgin C and a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

c. contacting non P gp/non MRP multidrug resistant cancer cells with a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

d. contacting said non P gp/non MRP multidrug resistant cancer cells with said test chemosensitizing reversal agent and a chemotherapeutic agent to which said cancer cells are resistant and measuring cancer cell death;

e.determining c. determining the presence and magnitude of BCRP or other non-P-gp/non MRP multiple drug resistance by comparing cancer cell death of step a to step b, and step c

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to step d wherein an increase in cancer cell death indicates higher levels of BCRP mediated or other non-P-gp/non MRP-multiple drug resistance.

25. (previously presented) The method according to claim 24 wherein the increase in cancer cell death by addition of the test chemosensitizing reversal agent is about 22% or above.

26. (original) The method according to claim 24 wherein the chemotherapeutic agent is

selected from the group consisting of mitoxantrone, doxorubicin, and topotecan.

27. (canceled)

28. (original) The method according to claim 27 wherein the chemosensitizing reversal agent

is administered prior to, concurrently with, or after administration of the chemotherapeutic

agent.

29-56. (canceled)

57-59. (canceled)

60-63. (canceled)